RECEIVED CENTRAL FAX CENTER

JAN 0 3 2008

Appl. No. 09/700,851 Response to Advisory Action Before the Filing of an Appeal Brief dated January 3, 2008

PATENT

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-4 (cancel)

- 5. (currently amended) A humanized antibody that is a humanized form of a mouse antibody characterized by a light chain variable region of SEQ ID NO:4 and a heavy chain variable region of SEQ ID NO:2, wherein the humanized antibody specifically binds to verotoxin II (VT2).
- 6. (previously presented) A humanized antibody that competes with a mouse antibody characterized by a light chain variable region of SEQ ID NO:4 and a heavy chain variable region of SEQ ID NO:2 for specific binding to VT2.
- 7. (currently amended) A humanized antibody of claim 5 comprising complementarity determining regions from the mouse antibody and heavy and light chain variable region frameworks from the human GF4 antibody heavy and light chain frameworks, provided that at least one position selected from the group consisting of L49, H29, H30, H49 and H98, is occupied by the amino acid present in the equivalent position of the mouse antibody heavy or light chain variable region framework, which humanized antibody specifically binds to verotoxin II with an affinity constant between 10⁷ M⁻¹ and ten-fold the affinity of the mouse VFmL1 antibody deposited as Accession No. FERM BP-10877.
- 8. (previously presented) The humanized antibody of claim 7, provided that each position selected from the group consisting of L49, 1129, 1130, 1149 and 1198 is occupied by the amino acid present in the equivalent position of the mouse antibody heavy or light chain variable region framework.

Appl. No. 09/700,851 Response to Advisory Action Before the Filing of an Appeal Brief dated January 3, 2008 PATENT

- 9. (original) The humanized antibody of claim 8, provided that at least one position selected from the group L3, L4, L19, L76, L79, L85, H1, H4, H5, H79, H89 and H93 is occupied by an amino acid present in the equivalent position of a human antibody heavy or light chain consensus sequence.
- 10. (original) The humanized antibody of claim 9, provided that each position selected from the group L3, L4, L19, L76, L79, L85, H1, H4, H5, H79, H89 and H93 is occupied by an amino acid present in the equivalent position of a human antibody heavy or light chain consensus sequence.
- 11. (previously presented) The humanized antibody of claim 5 comprising a heavy chain variable region of SEQ ID NO:6 and a light chain variable region of SEQ ID NO:8 provided that one or more positions selected from the group consisting of L49, H29, H30, H49, H98, L3, L4, L19, L76, L79, L85, H1, H4, H5, H79, H89 and H93 may be substituted as shown in Tables 2 and 3.
- 12. (previously presented) The humanized antibody of claim 5 comprising a heavy chain variable region of SEQ ID NO:6 and a light chain variable region of SEQ ID NO:8.
- 13. (currently amended) The humanized antibody of claim 5, comprising a humanized heavy chain having at least 85% identity with the humanized heavy chain of SEQ ID NO:6 and a humanized light chain having at least 85% sequence identity with the humanized light chain of SEQ ID NO:8, provided that at least one position selected from the group consisting of L49, H29, H30, H49 and H98, is occupied by the amino acid present in the equivalent position of the mouse VTmL1 antibody heavy or light chain variable region framework.

Appl. No. 09/700,851 Response to Advisory Action Before the Filing of an Appeal Brief dated January 3, 2008 PATENT

- 14. (previously presented) The humanized antibody of claim 5 or 6, wherein the antibody comprises two pairs of light/heavy chain dimers, wherein each chain comprises a variable region and a constant region.
- 15. (previously presented) The humanized antibody of claim 5 or 6, which is a Fab fragment or a F(ab')₂.
- 16. (previously presented) The humanized antibody of claim 5 or 6 in purified form.
- 17. (previously presented) The humanized antibody of claim 5 or 6, which has an IgG₁ immunoglobulin isotype.
- 18. (previously presented) A method of producing a humanized antibody, comprising culturing a cell line, which encodes heavy and light chain chains of the humanized antibody of claim 5 or 6, whereby the humanized antibody is expressed; and recovering the humanized antibody expressed by the cell line.
- 19. (original) The method of claim 18, further comprising mixing the antibody with a pharmaceutically acceptable carrier to produce a pharmaceutical composition.
- 20. (previously presented) A pharmaceutical composition comprising the humanized antibody of claim 5 or 6 and a pharmaceutically acceptable carrier.
- 21. (original) A pharmaceutical composition comprising the humanized antibody of claim 12 and a pharmaceutically acceptable earrier.

Appl. No. 09/700.851 Response to Advisory Action Before the Filing of an Appeal Brief dated January 3, 2008 PATENT

- 22. (previously presented) A method of treating a patient suffering or at risk of toxic effects from a verotoxin, comprising administering to the patient an effective dosage of a human or humanized antibody that specifically binds to verotoxin II, wherein the humanized antibody is as defined in claim 5 or claim 6.
- 23. (previously presented) The method of claim 22, wherein the antibody competes with a mouse antibody characterized by a light chain variable region of SEQ ID NO:4 and a heavy chain variable region of SEQ ID NO:2 for specific binding to VT2.
 - 24. (cancel)
- 25. (previously presented) The method of claim 22, wherein the humanized antibody specifically binds to the B subunit of VT2.

26-28. (cancel)

- 29. (previously presented) The method of claim 22, wherein the antibody is a humanized antibody comprising a heavy chain variable region of SEQ ID NO:6 and a light chain variable region of SEQ ID NO:8.
- 30. (original) The method of claim 22, wherein the patient is infected with verotoxin producing $E.\ coli$ and the antibody is administered therapeutically.
- 31. (original) The method of claim 22, wherein the patient is at risk of infection by verotoxin producing *E. coli* and the antibody is administered prophylactically.
- 32. (previously presented) The method of claim 30, further comprising monitoring the patient for recovery from the toxic effects of VT2.

Appl. No. 09/700,851 Response to Advisory Action Before the Filing of an Appeal Brief dated January 3, 2008 PATENT

33. (previously presented) A cell line that produces the antibody of claim 5 or 6.